

CLAIMS

1. A nucleic acid that is a non-naturally-occurring nucleic acid with a melting temperature that is at least 3°C higher than that of the corresponding control nucleic acid with 2'-deoxynucleotides; wherein said nucleic acid is capable of hybridizing to a first region within a first exon of a target nucleic acid and to a second region within a second exon of said target nucleic acid that is adjacent to said first exon.

2. A nucleic acid that is a non-naturally-occurring nucleic acid with a melting temperature that is at least 3°C higher than that of the corresponding control nucleic acid with 2'-deoxynucleotides; wherein said nucleic acid is capable of hybridizing to a first region within an exon of a target nucleic acid and to a second region within an intron of said target nucleic acid that is adjacent to said exon.

3. A nucleic acid that is a non-naturally-occurring nucleic acid with a melting temperature that is at least 3°C higher than that of the corresponding control nucleic acid with 2'-deoxynucleotides; wherein said nucleic acid is capable of hybridizing to a first region within a first intron of a target nucleic acid and to a second region within a second intron of said target nucleic acid that is adjacent to said first intron.

4. A nucleic acid that is a non-naturally-occurring nucleic acid with a capture efficiency that is at least 10% greater than that of a corresponding control nucleic acid with 2'-deoxynucleotides at the temperature equal to the melting temperature of said nucleic acid; wherein said nucleic acid is capable of hybridizing to a first region within a first exon of a target nucleic acid and to a second region within a second exon of said target nucleic acid that is adjacent to said first exon.

5. A nucleic acid that is a non-naturally-occurring nucleic acid with a capture efficiency that is at least 10% greater than that of a corresponding control nucleic acid with 2'-deoxynucleotides at the temperature equal to the melting temperature of said nucleic acid; wherein said nucleic acid is capable of hybridizing to a first region within an exon of a target

nucleic acid and to a second region within an intron of said target nucleic acid that is adjacent to said exon.

6. A nucleic acid that is a non-naturally-occurring nucleic acid with a capture efficiency that is at least 10% greater than that of a corresponding control nucleic acid with 2'-deoxynucleotides at the temperature equal to the melting temperature of said nucleic acid; wherein said nucleic acid is capable of hybridizing to a first region within a first intron of a target nucleic acid and to a second region within a second intron of said target nucleic acid that is adjacent to said first intron.

7. A nucleic acid that is an LNA capable of hybridizing to a first region within a first exon of a target nucleic acid and to a second region within a second exon of said target nucleic acid that is adjacent to said first exon.

8. A nucleic acid that is an LNA capable of hybridizing to a first region within an exon of a target nucleic acid and to a second region within an intron of said target nucleic acid that is adjacent to said exon.

9. A nucleic acid that is an LNA capable of hybridizing to a first region within a first intron of a target nucleic acid and to a second region within a second intron of said target nucleic acid that is adjacent to said first intron.

10. The nucleic acid of any one of claims 1-9, wherein the length of said first region and the length of said second region are between 3 and 50 nucleotides, inclusive.

11. The nucleic acid of claim 10, wherein the length of said first region and the length of said second region are between 10 and 40 nucleotides, inclusive.

12. The nucleic acid of claim 11, wherein the length of said first region and the length of said second region are between 20 and 30 nucleotides, inclusive.

13. The nucleic acid of any one of claims 1-9, wherein said first region and said second region are the same length.

5 14. The nucleic acid of any one of claims 1-9, wherein said first region and said second region are a different length.

15. A population of nucleic acids that includes a nucleic acid of any one of claims 1-14.

10 16. A population of nucleic acids that includes a non-naturally-occurring nucleic acid with a melting temperature that is at least 3°C higher than that of the corresponding control nucleic acid with 2'-deoxynucleotides; wherein said nucleic acid is capable of hybridizing to only one exon or to only one intron of a target nucleic acid.

15 17. A population of nucleic acids that includes a non-naturally-occurring nucleic acid with a capture efficiency that is at least 10% greater than that of a corresponding control nucleic acid with 2'-deoxynucleotides at the temperature equal to the melting temperature of said nucleic acid; wherein said nucleic acid is capable of hybridizing to only one exon or to only one intron of a target nucleic acid.

20 18. A population of nucleic acids that includes a nucleic acid that is an LNA capable of hybridizing to only one exon or to only one intron of a target nucleic acid.

25 19. A nucleic acid of any one of claims 1-9 that is a non-naturally occurring nucleic acid with a melting temperature that is at least 3°C higher than that of the corresponding control nucleic acid with 2'-deoxynucleotides; wherein said nucleic acid is capable of hybridizing to only one exon or to only one intron of a target nucleic acid.

30 20. A nucleic acid of any one of claims 1-9 that is a non-naturally-occurring nucleic acid with a capture efficiency that is at least 10% greater than that of a corresponding control nucleic acid with 2'-deoxynucleotides at the temperature equal to the melting temperature of said

nucleic acid; wherein said nucleic acid is capable of hybridizing to only one exon or to only one intron of a target nucleic acid.

21. A nucleic acid of any one of claims 1-9 that comprises an LNA capable of
5 hybridizing to only one exon or to only one intron of a target nucleic acid.

22. The population of any one of claims 15-18, wherein said nucleic acid is between 15
and 150 nucleotides in length, inclusive.

10 23. The population of claim 22, wherein said nucleic acid is between 5 and 100
nucleotides in length, inclusive.

24. The population of claim 23, wherein said nucleic acid is between 20 and 80
nucleotides in length, inclusive.

15 25. The population of claim 24, wherein said nucleic acid is between 30 and 60
nucleotides in length, inclusive.

26. The population of claim 25, wherein said nucleic acid is 40 nucleotides in length.

20 27. The population of claim 25, wherein said nucleic acid is 50 nucleotides in length.

28. The nucleic acid of any one of claims 1-9 and 19-21 wherein said nucleic acid is
between 8 and 70 nucleotides in length.

25 29. The nucleic acid of any one of claims 1-9 and 19-21 wherein said nucleic acid is
between 9 and 50 nucleotides in length.

30 30. The nucleic acid of any one of claims 1-9 and 19-21 wherein said nucleic acid is
between 12 and 40 nucleotides in length.

31. The nucleic acid of any one of claims 1-9 and 19-21 wherein said nucleic acid is between 15 and 35 nucleotides in length.

5 32. The population of any one of claims 15-18, wherein at least 5% of the nucleotides in said nucleic acid are LNA units.

33. The population of claim 32, wherein at least 10% of the nucleotides in said nucleic acid are LNA units.

10 34. The population of claim 32, wherein at least 20% of the nucleotides in said nucleic acid are LNA units.

15 35. The population of any one of claims 15-18, wherein every second nucleotide in said nucleic acid is an LNA unit.

36. The population of any one of claims 15-18, wherein every third nucleotide in said nucleic acid is an LNA unit.

20 37. The population of any one of claims 15-18, wherein every fourth nucleotide in said nucleic acid is an LNA unit.

38. The population of any one of claims 15-18, wherein every fifth nucleotide in said nucleic acid is an LNA unit.

25 39. The population of any one of claims 15-18, wherein every sixth nucleotide in said nucleic acid is an LNA unit.

30 40. The population of any one of claims 15-18, wherein (i) every second and every third nucleotide, (ii) every second and every fourth nucleotide, (iii) every second and every fifth nucleotide, (iv) every second and every sixth nucleotide, (v) every third and every fourth nucleotide, (vi) every third and every fifth nucleotide, (vii) every third and every sixth

nucleotide, (viii) every fourth and every fifth nucleotide, (ix) every fourth and every sixth nucleotide, and/or (x) every fifth and every sixth nucleotide in said nucleic acid is an LNA unit.

41. The population of claim 40, wherein every second, every third, and every fourth
5 nucleotide in said nucleic acid is an LNA unit.

42. The population of any one of claims 15-18, wherein said nucleic acid comprises two or more contiguous LNA units.

10 43. The population of claim 42, wherein said nucleic acid comprises at least 4 contiguous LNA units.

44. The population of claim 42, wherein said nucleic acid comprises at least 5 contiguous LNA units.

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45. The population of claim 42, wherein the number of contiguous LNA units is between 5 and 20% of the total length of said nucleic acid.

20 46. The population of claim 45, wherein the number of contiguous LNA units is between 10 and 15% of the total length of said nucleic acid.

47. The population of claim 42, wherein at least one LNA unit in said nucleic acid is capable of hybridizing to a first region within a first exon of a target nucleic acid and at least one LNA unit in said nucleic acid is capable of hybridizing to a second region within a second exon
25 of said target nucleic acid that is adjacent to said first exon.

48. The population of claim 47, wherein at least two LNA units in said nucleic acid hybridize to a first region within a first exon of a target nucleic acid and at least two LNA units in said nucleic acid hybridize to a second region within a second exon of said target nucleic acid
30 that is adjacent to said first exon.

49. The population of claim 48, wherein at least three LNA units in said nucleic acid hybridize to a first region within a first exon of a target nucleic acid and at least three LNA units in said nucleic acid hybridize to a second region within a second exon of said target nucleic acid that is adjacent to said first exon.

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50. The population of any one of claims 15-18, wherein the 5' terminal nucleotide of said nucleic acid is not an LNA unit.

51. The population of any one of claims 15-18, wherein the 5' terminal nucleotide of
10 said nucleic acid is an LNA unit.

52. The population of any one of claims 15-18, wherein the 3' terminal nucleotide of said nucleic acid is not an LNA unit.

15 53. The population of any one of claims 15-18, wherein said nucleic acid can distinguish between different nucleic acids that cannot be distinguished using a naturally-occurring control nucleic acid.

54. The population of claim 53, wherein said control nucleic acid consists of only 2'-
20 deoxynucleotides.

55. The population of claim 53, wherein said different nucleic acids are mRNA splice variants.

25 56. The population of any one of claims 15-18, wherein said nucleic acid comprises one or more universal bases.

57. The population of claim 56, wherein said universal base is located at the 5' or 3' terminus of said nucleic acid.

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58. The population of claim 56, wherein one or more universal base are located at the 5' and 3' termini of said nucleic acid.

59. The population of claim 56, wherein all of said nucleic acids of said population have the same number of universal bases.

60. The population of claim 56, wherein said universal base is inosine, pyrene, 3-nitropyrrole, or 5-nitroindole.

61. The population of any one of claims 15-18, wherein said nucleic acid comprises at least one LNA A or LNA T.

62. The population of any one of claims 15-18, wherein each nucleic acid in said population comprises at least one LNA A or LNA T.

63. The population of claim 61, wherein all of the adenine and thymine-containing nucleotides in said LNA are LNA A and LNA T, respectively.

64. The population of any one of claims 15-18, wherein said nucleic acid comprises at least one 2,6-diaminopurine or 2-thio-thymine base.

65. The population of any one of claims 15-18, wherein at least 5% of the nucleic acids in said population are LNA.

66. The population of any one of claims 15-18, wherein at least 10% of the nucleic acid in said population are LNA.

67. The population of any one of claims 15-18, that includes nucleic acids that together hybridize to at least 10% of the nucleic acids expressed by a particular cell or tissue.

68. The population of claim 67, that includes nucleic acids that together hybridize to at least 50% of the exons of a target nucleic acid.

69. The population of any one of claims 15-18, wherein said nucleic acid does not form a hairpin that would otherwise inhibit its binding to a target nucleic acid.

70. The population of any one of claims 15-18, wherein opposing nucleotides in a palindrome pair or opposing nucleotides in inverted repeats of said nucleic acid are not both LNA units.

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71. The population of any one of claims 15-18, wherein said nucleic acid forms less than 3 intramolecular base-pairs.

72. The population of any one of claims 15-18, wherein said nucleic acid does not have LNA-5-nitroindole: LNA-5-nitroindole intramolecular base-pairs.

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73. The population of any one of claims 15-18, wherein said nucleic acid has a LNA unit with a 2,6,-diaminopurine, 2-aminopurine, 2-thio-thymine, 2-thio-uracil, inosine, or hypoxanthine base.

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74. The population of any one of claims 15-18, wherein said nucleic acid has a 2'O, 4'C-methylene linkage.

75. The population of any one of claims 15-18, wherein one or more nucleic acids are LNA/DNA, LNA/RNA, or LNA/DNA/RNA chimeras.

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76. The population of any one of claims 15-18, wherein said nucleic acid has a melting temperature that is at least 10°C higher than that of the corresponding control nucleic acid with 2'-deoxynucleotides.

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77. The population of claim 76, wherein said nucleic acid has a melting temperature that is at least 20°C higher than that of the corresponding control nucleic acid with 2'-deoxynucleotides.

5 78. The population of any one of claims 15-18, wherein said nucleic acid has a capture efficiency that is at least 100% greater than that of the corresponding control nucleic acid with 2'-deoxynucleotides at the temperature equal to the melting temperature of said nucleic acid.

10 79. The population of claim 78, wherein said nucleic acid has a capture efficiency that is at least 400% greater than that of the corresponding control nucleic acid with 2'-deoxynucleotides at the temperature equal to the melting temperature of said nucleic acid.

15 80. The population of any one of claims 15-18, wherein said nucleic acids are covalently bonded to a solid support.

81. The population of claim 80, wherein said nucleic acids are in a predefined arrangement.

20 82. The population of any one of claims 15-18, comprising at least 10 different nucleic acids.

83. The population of claims 82, comprising at least 100 different nucleic acids.

25 84. The population of claim 83, comprising at least 500 different nucleic acids.

85. The population of claim 84, comprising at least 1,000 different nucleic acids.

86. The population of claim 85, comprising at least 5,000 different nucleic acids.

87. A complex of one or more target nucleic acids and one or more nucleic acids or populations of any one of claims 1-9, 15-18 or 19-21 in which one or more target nucleic acids are hybridized to one or more said nucleic acids or populations.

5 88. The complex of claim 87, wherein at least 10 different target nucleic acids are hybridized.

89. The complex of claim 87, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample.

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90. The complex of claim 87, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase.

15 91. The complex of claim 87, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 300 nucleotides.

20 92. The complex of claim 87, wherein the target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 200 nucleotides.

25 93. The complex of claim 87, wherein the target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 100 nucleotides.

94. The complex of claim 87, wherein the target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 50 nucleotides.

30 95. The complex of claim 87, wherein said target nucleic acids are cRNA molecules amplified from a sample.

96. The complex of claim 87, wherein said target nucleic acids are cRNA molecules amplified from a sample and fragmented using alkaline hydrolysis.

5 97. The complex of claim 87, wherein at least 10 different target nucleic acids are labeled and hybridized.

98. The complex of claim 87, wherein said target nucleic acids are RNA molecules isolated from a sample and labeled chemically directly, e.g. using platinum-linked fluorescent
10 dyes.

99. The complex of claim 87, wherein said target nucleic acids are RNA molecules isolated from a sample and labeled chemically directly, e.g. using platinum-linked fluorescent dyes and fragmented using alkaline hydrolysis.

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100. A method for detecting the presence of one or more target nucleic acids in a sample, said method comprising incubating a labeled nucleic acid sample with one or more first nucleic acids of any one of claims 1-9 or 19-21 or one or more populations of first nucleic acids of any one of claims 15-18 under conditions that allow at least one target nucleic acid to hybridize to at
20 least one of said first nucleic acids.

101. The method of claim 100, wherein hybridization is detected between at least 5 target nucleic acids and said first nucleic acids.

25 102. The method of claim 100, further comprising identifying one or more hybridized target nucleic acids.

103. The method of claim 100, further comprising determining the amount of one or more hybridized target nucleic acids.

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104. The method of claim 100, wherein one or more target nucleic acids are labeled with a fluorescent group, and wherein the determination of the amount of said hybridized target nucleic acid involves one or more of the following: (i) adjusting for the varying intensity of an excitation light source used for detection of said hybridization, (ii) adjusting for photobleaching of said fluorescent group, and/or (iii) comparing the fluorescent intensity of said hybridized target nucleic acid(s) to the fluorescent intensity of a different sample of hybridized nucleic acids.

105. The method of claim 100, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample.

106. The method of claim 105, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase.

107. The method of claim 105, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 300 nucleotides.

108. The method of claim 105, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 200 nucleotides.

109. The method of claim 105, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 100 nucleotides.

110. The method of claim 105, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 50 nucleotides.

111. The method of claim 105, wherein said target nucleic acids are cRNA molecules amplified from a sample that is optionally fragmented using alkaline hydrolysis.

112. The method of claim 100, further comprising determining the presence or absence of an mRNA splice variant of interest in said sample or determining the presence or absence of a mutation, deletion, and/or duplication of an exon of interest.

113. The method of claim 100, wherein the sample has nucleic acids that are amplified using one or more primers specific for an exon of a target nucleic acid, and wherein said method involves determining the presence or absence of an mRNA splice variant with said exon in said sample.

114. The method of claim 113, wherein one or more of said primers are specific for an exon or exon-exon junction of interest, and said method involves determining the presence or absence of a nucleic acid with said exon in said sample.

115. The method of claim 100, wherein said first nucleic acids are covalently bonded to a solid support by reaction of a nucleoside phosphoramidite with an activated solid support, and subsequent reaction of a nucleoside phosphoramidite with an activated nucleotide or nucleic acid bound to said solid support.

116. The method of claim 100, further comprising contacting said target nucleic acid with a second nucleic acid or a population of second nucleic acids that binds to a different region of the target molecule than said first nucleic acid.

117. A method for amplifying a target nucleic acid, said method comprising the steps of: (a) incubating one or more first nucleic acids of any one of claims 1-9 or 19-21 or one or more populations of first nucleic acids of any one of claims 15-18 with a target nucleic acid under conditions that allow said first nucleic acid to bind said target nucleic acid; and (b) extending said first nucleic acid with said target nucleic acid as a template.

118. The method of claim 117, further comprising contacting said target nucleic acid with a second nucleic acid or a population of second nucleic acids that binds to a different region of the target molecule than said first nucleic acid.

5 119. A method for classifying a test nucleic acid sample comprising a target nucleic acid, said method comprising the steps of: (a) incubating a test nucleic acid sample with one or more nucleic acids probes of any one of claims 1-9 or 19-21 or one or more populations of nucleic acids probes of any one of claims 15-18 under conditions that allow at least one of the nucleic acids in said test sample to hybridize to at least one nucleic acid probe; (b) detecting a
10 hybridization pattern of said test nucleic acid sample; and (c) comparing said hybridization pattern to a hybridization pattern of a first nucleic acid standard, whereby said comparison indicates whether or not said test sample has the same classification as said first standard.

120. The method of claim 119, further comprising comparing a hybridization pattern of
15 said test nucleic acid sample to a hybridization pattern of a second standard.

121. The method of claim 119, wherein at least 5 target nucleic acids hybridize to said nucleic acid probes.

20 122. The method of claim 119, further comprising identifying a hybridized target nucleic acid.

123. The method of claim 119, further comprising determining the amount of said hybridized target nucleic acid.

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124. The method of claim 119, wherein said target nucleic acids are labeled with fluorescent groups.

125. The method of claim 124, wherein said determination comprises scaling for the
30 varying labeling efficiency for the different fluorescent groups used for detection of said hybridization.

126. The method of claim 124, wherein said determination comprises adjusting for the varying intensity of the excitation light source used for detection of said hybridization.

5 127. The method of claim 124, wherein said determination comprises adjusting for photobleaching of said fluorescent group.

128. The method of claim 124, wherein said comparison comprises adjusting for a difference in the amount of said nucleic acid probes used for hybridization to said test sample
10 and said first standard.

129. The method of claim 124, wherein said comparison comprises adjusting for a difference in the buffer used for hybridization to said test sample and said first standard.

15 130. The method of claim 129, wherein said difference is a difference in Na^+ concentration.

131. The method of claim 124, wherein said first nucleic acid standard is labeled with a different fluorescent group.
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132. The method of claim 119, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and optionally fragmented using *E. coli* Uracil-DNA Glycosylase.

25 133. The method of claim 119, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 300 nucleotides.

30 134. The method of claim 119, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 200 nucleotides.

135. The method of claim 119, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 100 nucleotides.

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136. The method of claim 119, wherein said target nucleic acids are cDNA molecules reverse transcribed from a sample and fragmented using *E. coli* Uracil-DNA Glycosylase to an average size of 50 nucleotides.

10 137. The method of claim 119, wherein said target nucleic acids are cRNA molecules amplified from a sample.

138. The method of claim 119, wherein said target nucleic acids are cRNA molecules amplified from a sample and fragmented using alkaline hydrolysis.

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139. The method of claim 119, further comprising determining the presence or absence of an mRNA splice variant of interest in said sample.

140. The method of claim 119, further comprising determining the presence or absence
20 of a mutation, deletion, and/or duplication of an exon of interest.

141. The method of claim 140, wherein said mutation, deletion, and/or duplication is indicative of a disease, disorder, or condition.

25 142. The method of claim 141, wherein said disease is cancer.

143. The method of claim 119, wherein the sample has nucleic acids that are amplified using one or more primers specific for an exon of a target nucleic acid, and wherein said method involves determining the presence or absence of an mRNA splice variant with said exon in said
30 sample.

144. The method of claim 143, wherein one or more of said primers are specific for an exon or exon-exon junction of interest, and said method involves determining the presence or absence of a nucleic acid with said exon in said sample.

145. The method of claim 119, wherein said first nucleic acids are covalently bonded to a solid support by reaction of a nucleoside phosphoramidite with an activated solid support, and subsequent reaction of a nucleoside phosphoramidite with an activated nucleotide or nucleic acid bound to said solid support.

146. A method of selecting a nucleic acid for a population of nucleic acids, said method comprising the steps of: (a) determining the melting temperature of a nucleic acid, determining the ability of said nucleic acid to self-anneal, determining the ability of said nucleic acid to hybridize to one or more exons or introns of a target nucleic acid, and/or determining the ability of said nucleic acid to hybridize to a non-target nucleic acid, and (b) selecting said nucleic acid for inclusion or exclusion from said population based on the determination in step (a), wherein said nucleic acid is a nucleic acid of any one of claims 1-9 or 19-21 or a nucleic acid that has least one LNA unit and that is capable of hybridizing to only one exon or to only one intron of a target nucleic acid.

147. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 for the detection, amplification, or classification of a nucleic acid of interest or a population of nucleic acids of interest.

148. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 for alternative mRNA splice variant detection, expression profiling, comparative genomic hybridization, or real-time PCR.

149. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 as a PCR primer or FISH probe.

150. Use according to claim 149 wherein said nucleic acid or said population of nucleic acids comprise LNA in about every other or about every third position of the nucleotide sequence.

5 151. Use according to claim 149 wherein said nucleic acid or said population of nucleic acids are used for the detection of a repetitive element.

152. Use according to claim 151 wherein said repetitive element is a centromeric alpha-repeat or a telomeric repeat.

10 153. Use according to claim 149 wherein said nucleic acid or said population of nucleic acids are used for the detection of a single base pair difference between repetitive sequences or for the detection of single copy sequences.

15 154. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 as a probe in fluorescent in situ hybridisation of a target DNA without a denaturation step.

20 155. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 in a homogeneous assay such as quantitative real-time RT-PCR assay, e.g. Taqman real-time RT-PCR, Lightcycler real-time RT-PCR , or real-time NASBA (nucleic acid sequence-based amplification) assay with a Molecular Beacon-based detection.

25 156. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 in a diagnostic kit based on a homogeneous assay such as quantitative real-time RT-PCR assay, e.g. Taqman real-time RT-PCR, Lightcycler real-time RT-PCR , or real-time NASBA (nucleic acid sequence-based amplification) assay with a Molecular Beacon-based detection.

30 157. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 as an antisense, antigene or ribozyme or double stranded

nucleic acid therapeutic agent, or in therapeutic use as modulating and silencing sense nucleic acid agents.

5 158. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 as an antisense, antigene or ribozyme or double stranded nucleic acid therapeutic agent, in which the said nucleic acid or population of nucleic acids hybridize to specific splice isoforms or isoforms.

10 159. Use of a nucleic acid or a population of nucleic acids of any one of claims 1-9 or 19-21 or of claims 15-18 as an antisense, antigene or ribozyme or double stranded nucleic acid therapeutic agent, in which the said nucleic acid or population of nucleic acids hybridize to a non-coding antisense RNA or RNAs.

15 160. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 in a diagnostic kit, based on detection of diagnostic splice isoforms or splice patterns, or diagnostic nucleic acids, such as viral or bacterial mRNAs.

20 161. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 in a diagnostic microarray based on detection of mRNA signatures or splice isoform signatures in the concentration range of 10000 ppm to 1000 ppm.

25 162. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 in a diagnostic microarray based on detection of mRNA signatures or splice isoform signatures in the concentration range of 1000 ppm to 100 ppm.

163. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 in a diagnostic microarray based on detection of mRNA signatures or splice isoform signatures in the concentration range of 100 ppm to 10 ppm.

164. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 in a diagnostic microarray based on detection of mRNA signatures or splice isoform signatures in the concentration range of 10 ppm to 1 ppm.

5 165. Use of a nucleic acid of any one of claims 1-9 or 19-21 or a population of nucleic acids of any one of claims 15-18 in a diagnostic microarray based on detection of mRNA signatures or splice isoform signatures.

10 166. Use of a non-naturally occurring nucleic acid of any one of claims 1-9 or 19-21 or use of a population of non-naturally occurring nucleic acids of any one of claims 15-18 in a method for generating an array of said non-naturally occurring nucleic acids of chosen lengths within discrete locations of a support material.

15 167. Use according to claim 166, where said non-naturally occurring nucleic acids are LNA oligonucleotides.

20 168. Use according to any one of claims 166-167, where said non-naturally occurring nucleic acids are LNA oligonucleotides containing a photochemically active group at the 5' end or the 3' end, separated by a linker from the LNA oligonucleotides.

25 169. Use according to any one of claims 166-168, wherein said linker is a hexaethylene monomer, dimer, trimer, tetramer, pentamer or hexamer, or a poly-T sequence of 10-50 nucleotides in length, or a poly-C sequence of 10-50 nucleotides in length.

30 170. Use according to any one of claims 168-169 for generating an array comprising the steps of a) selecting said nucleic acid or population of nucleic acids according to the method of claim 146, b) synthesis of the said nucleic acids using phosphoramidite chemistry and DNA and LNA phosphoramidites; c) purification of the said nucleic acids; d) printing of the said nucleic acids of chosen lengths and sequence onto a polymer surface; and e) coupling of said nucleic acids via excitation of the photochemically active group at the 5' end or the 3' end covalently onto the polymer surface using UV light.

171. The method of claims 166-170 wherein a computer-controlled microarray printing robot delivers the said nucleic acids onto discrete locations on the polymer surface.

5 172. The method of claims 166-171, wherein the size of each discrete location is between an average size of 10 and 150 microns.

173. The method of claims 166-172, wherein said nucleic acids are printed at a density of at least 50 nucleic acids per square cm.

10 174. The method of claims 166-172, wherein said nucleic acids are printed at a density of at least 100 nucleic acids per square cm.

175. The method of claims 166-172, wherein said nucleic acids are printed at a density of at least 500 nucleic acids per square cm.

176. The method of claims 166-172, wherein said nucleic acids are printed at a density of at least 1000 nucleic acids per square cm.

20 177. The method of claims 166-172, wherein said nucleic acids are printed at a density of at least 2500 nucleic acids per square cm.

178. The method of claims 166-172, wherein said nucleic acids are printed at a density of at least 4000 nucleic acids per square cm.

25 179. The method of claims 166-172, wherein said nucleic acids are printed at a density of at least 10000 nucleic acids per square cm.

180. The method of claim 139, wherein said mRNA splice variant is indicative of a disease, disorder, or condition.

181. The method of claim 180, wherein said disease is cancer.

182. Use according to claim 149 wherein said nucleic acid or said population of
nucleic acids are used for the detection of a repetitive element in human chromosomes 13 and
5 21.

183. Use according to claim 153 wherein said nucleic acid or said population of
nucleic acids are used for the detection of a single base pair difference between repetitive
sequences of human chromosomes 13 and 21.

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184. Use according to claim 183 wherein said repetitive element is a centromeric
alpha-repeat.